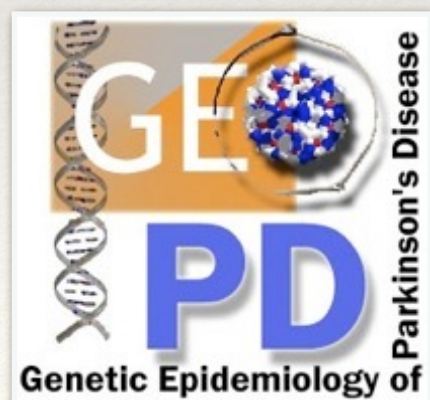*Longitudinal Clinical and Genetic Study of Parkinson's Disease*

The LONG-PD Study: Leading the World to Predict and Improve Outcomes in Parkinson's Disease

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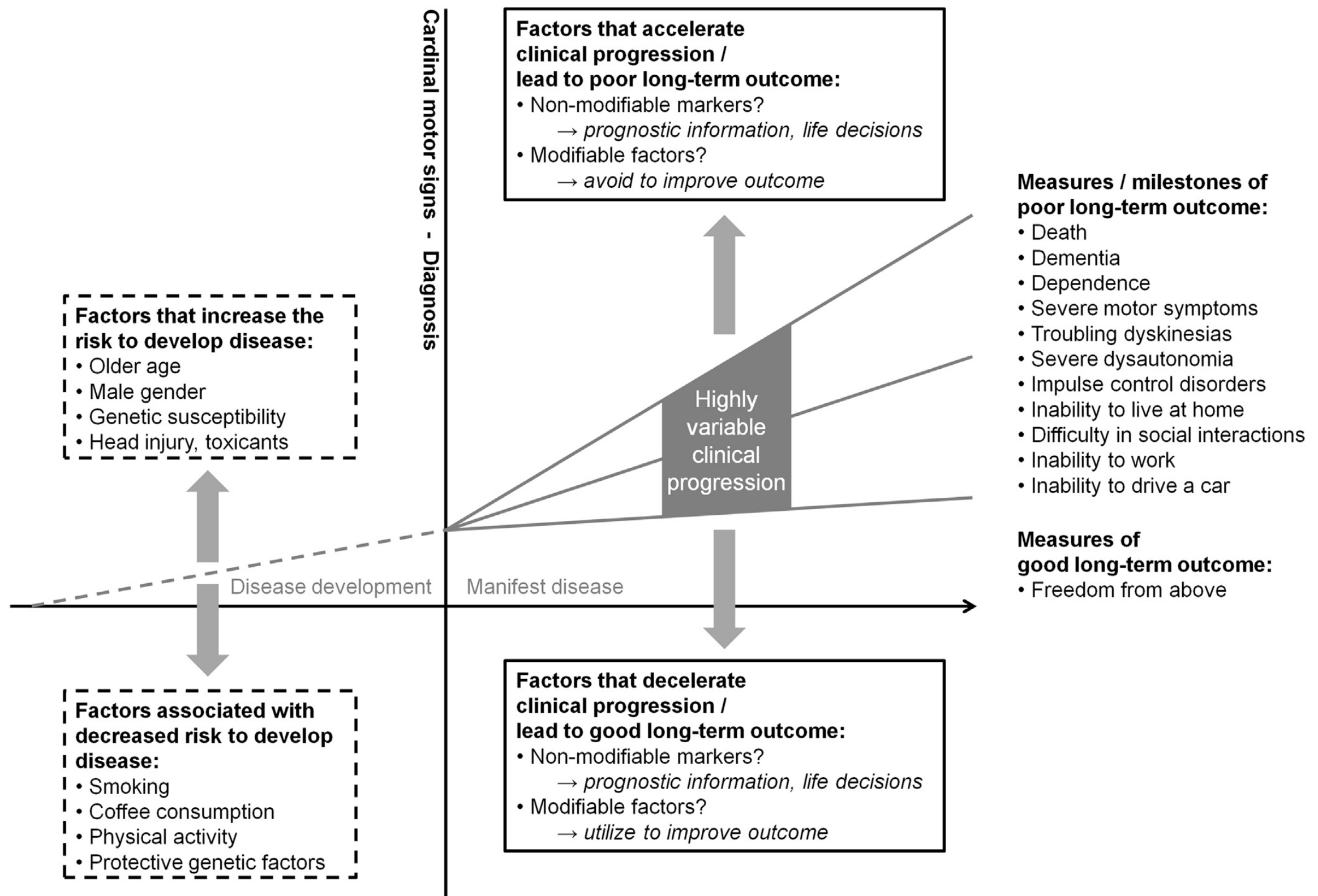Evanston, IL USA

Progression and Outcomes in Parkinson's Disease

- Motor Progression
  - 9-Hole Peg Test
  - UPDRS Motor score
  - Hoehn and Yahr Stage
  - Activities of Daily Living (UPDRS, Schwab & England)
- Non-Motor Progression
  - Montreal Cognitive Assessment
  - Geriatric Depression Scale
  - Epworth Sleepiness Scale
  - UPDRS Mentation, Behavior, Mood
- Complications of Therapy
  - Dyskinesias, Fluctuations, Other
- Nursing Home Placement (7x risk)
- Death (2x risk)
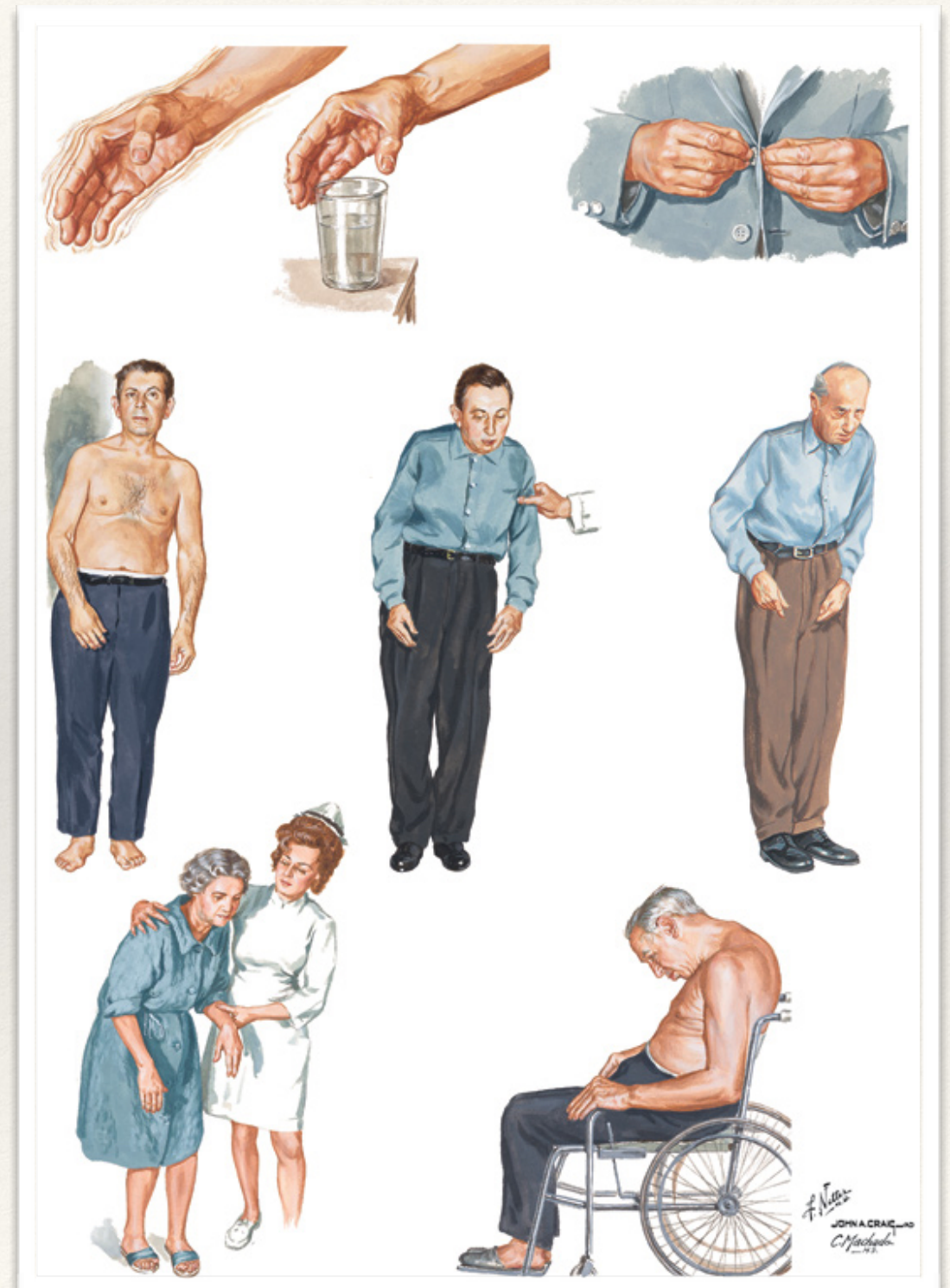
Background

- Neurologists worldwide assess progression and outcomes for millions of PD patients yearly; but the measures are not standardized across practices or available for collaborative studies

- Clinical or genetic factors that influence motor and non-motor progression and outcomes in PD are unknown

- Identification of those factors may allow us to individualize the care of patients and to improve neurological health

Cardinal motor signs - Diagnosis

Factors that accelerate clinical progression / lead to poor long-term outcome:
- Non-modifiable markers?
    → *prognostic information, life decisions*
- Modifiable factors?
    → *avoid to improve outcome*

Factors that increase the risk to develop disease:
- Older age
- Male gender
- Genetic susceptibility
- Head injury, toxicants

Measures / milestones of poor long-term outcome:
- Death
- Dementia
- Dependence
- Severe motor symptoms
- Troubling dyskinesias
- Severe dysautonomia
- Impulse control disorders
- Inability to live at home
- Difficulty in social interactions
- Inability to work
- Inability to drive a car

Measures of good long-term outcome:
- Freedom from above

Highly variable clinical progression

Disease development   Manifest disease

Factors associated with decreased risk to develop disease:
- Smoking
- Coffee consumption
- Physical activity
- Protective genetic factors

Factors that decelerate clinical progression / lead to good long-term outcome:
- Non-modifiable markers?
    → *prognostic information, life decisions*
- Modifiable factors?
    → *utilize to improve outcome*

Hypothesis

The factors that increase PD risk are different from the factors that accelerate disease progression or lead to poor long-term outcomes

Aims

❖ To develop web-based tools for the capture and sharing of data that measure motor and non-motor progression and outcomes in PD

❖ To share DNAs in a central repository (separate from the data coordinating site)

❖ To conduct clinical and genetic studies of progression and outcomes in PD

REDCap (Overview)

- REDCap is a web-based tool designed for the electronic capture and sharing of data (http://project-redcap.org/)

- REDCap is employed by 1,499 institutions in 91 countries for more than 176,000 projects with over 241,000 users

- Data are captured and stored and managed centrally, but access can be sequestered by site

- De-identification, access restriction, data logging/auditing, and secure data transfer features protect human subjects

REDCap (Features)

❖ Stream-lined process for rapidly building a database or online survey

❖ Advanced features: branch logic, file uploading, and calculated fields

❖ Quick and easy software installation process

❖ Interface for collecting and validating data, including mobile devices

❖ Automated export of data to statistical packages (SPSS, SAS, Stata, R)

❖ Custom reports, data visualization, data cleaning, and analysis tools

❖ Archiving of forms (IRB approvals, consents, data use agreements)

❖ Study visit scheduling and e-communication tools

Preliminary Studies (GEO-PD)

❖ GEO-PD includes 60 sites from 30 countries and 6 continents, sharing DNA and data for 41,988 PD cases and 41,505 controls; we meet annually and published >20 papers/10 yrs

❖ 25 sites from 18 countries and 5 continents are willing to share for 100+ PD cases, DNAs and motor and cognitive outcomes data collected annually for 15 yrs

❖ We expect to enroll at least 4,200 PD cases

Site PI	Country	Continent	Targeted enrollment
AASLY	NORWAY	EUROPE	100
BERG	GERMANY	EUROPE	100
BRIGHINA	ITALY	EUROPE	100
CARR	SOUTH AFRICA	AFRICA	100
CHUNG	KOREA	ASIA	500
CRAS	BELGIUM	EUROPE	100
CRESSWELL	CANADA	NORTH AMERICA	100
DESTEE	FRANCE	EUROPE	200
HADJIGEORGIOU	GREECE	EUROPE	100
HASSAN	USA	NORTH AMERICA	100
HATTORI	JAPAN	ASIA	200
HAQ	USA	NORTH AMERICA	100
KASTEN	GERMANY	EUROPE	100
KIM	KOREA	ASIA	100
KOKS	ESTONIA	EUROPE	100
KRUEGER	LUXEMBOURG	EUROPE	200
MARAGANORE	USA	NORTH AMERICA	1,000
MELLICK	AUSTRALIA	AUSTRALIA	100
SAZCI	TURKEY	EUROPE	100
TAN	SINGAPORE	ASIA	100
TOFT	NORWAY	EUROPE	100
WIDER	SWITZERLAND	EUROPE	100
WIRDEFELDT	SWEDEN	EUROPE	100
WOITALLA	GERMANY	EUROPE	100
ZESIEWICZ	USA	NORTH AMERICA	200

Preliminary Studies (NorthShore)

- NorthShore is conducting longitudinal clinical and genetic studies of 11 neurological disorders, including PD ("DodoNA Project: DNA Predictions to Improve Neurological Health")

- We built into our electronic medical record (Epic) structured clinical documentation support (SCDS) tools that standardize clinical care and write progress notes

- The SCDS tools capture ~1,000 discrete data per office visit

- We are banking DNAs for 1,000 patients/cohort (11,000 total)

- We enrolled ~475/1,000 PD cases, with 5+ years follows up

Methods (Pre-Enrollment)

❖ Northshore built a REDCap form mirroring its SCDS form

❖ A working group refined the form, defined required fields

❖ NorthShore finalized the form, presented it to GEO-PD

❖ Additional clinical and biorepository sites were recruited

❖ We are executing Data Use Agreements (DUAs)

❖ We will archive DUAs, IRB approvals, protocols, consents

Our REDCap Form

Methods (Enrollment, Follow Up)

❖ We will enroll consecutive PD cases with <5 yrs motor symptoms

❖ Targeted enrollment will be 100 PD cases per site, but without caps

❖ DNAs will be banked on accrual

❖ Data will be entered in REDCap on accrual

❖ NorthShore will clean data and generate monthly progress reports

❖ Follow up and data sharing will be ongoing for up to 15 yrs

❖ Genotyping and analyses at times 0, 5, 10, and 15 yrs

Timeline

- Recruitment of sites and screening for eligibility [Done]

- Drafting of REDCap form to mirror the NorthShore SCDS form [Done]

- Working Group to review and revise the draft REDCap form and study methods [Done]

- Presentation of REDCap form to GEO-PD at the 2014 annual meeting [Done]

- Finalize the REDCap form after the GEO-PD 2014 annual meeting [Done]

- Final recruitment of participating GEO-PD sites [Done]

- Designation of biobank(s) for centralized storing of DNAs and genotyping [Done]

- Publish consensus paper on longitudinal clinical and genetic studies of PD [Done]

- Execute DUAs, archive IRB approvals, protocols, and consents for each sites [July 1, 2015]

- Start date for enrollment of PD cases, biospecimens and data sharing [July 1, 2015]

- Targeted enrollment of 100+ PD cases per site (DNA and baseline data available) [July 1, 2017]

- Annual follow up visits for up to 15 years; optional enrollment of additional PD cases [2016-2031]

- Genotyping and data analyses at baseline, 5, 10, and 15 yrs; related publications [2015-2035]

Comparisons to the Michael J. Fox Foundation Parkinson's Progression Markers Initiative

Attribute	PPMI	LONG-PD
Sample size	400 PD cases	4,200 PD cases
Follow up	5 years	15 years
Person-years	2,000	63,000
Cohorts	de novo (<2 yrs)	all comers (<5 yrs)
Sites	21	25
Countries	6	18
Continents	2	5
Assessments	high-tech	pragmatic
Burden to participants	high (multiple visits)	low (point of care)
Risks	moderate (invasive)	low (non invasive)
Costs	$$ millions	unbudgeted
Sources of funds	MJFF, Pharma	academic

Significance and Innovation

❖ GEO-PD will discover clinical and genetic factors that predict progression and outcomes in PD

❖ GEO-PD's size and diversity are differentiating, making it an ideal replication engine for similar studies

❖ We will develop DNA tests that guide secondary prevention strategies (personalized medicine)

CONCORDIA DOMI FORIS PAX

Harmony within, peace without

LONG-PD

On behalf of the GEO-PD Consortium and NorthShore University HealthSystem

Parkinson Research at NorthShore

- **DodoNA Project: DNA Predictions to Improve Neurological Health** (Maraganore)

  - NorthShore Neurological Institute/Auxiliary funds

- **LONG-PD: Longitudinal Clinical and Genetic Studies of Parkinson's Disease** (Maraganore)

  - GEO-PD Consortium/NorthShore funds

- **Quality Improvement & Practice Based Research in Neurology Using the EMR** (Maraganore)

  - Neurology Practice Based Research Network/Agency for Healthcare Research and Quality

- **Imaging Biomarkers of Delayed Sequelae in Mild Traumatic Brain Injury** (Maraganore)

  - NorthShore Neurological Institute /GE Healthcare funds

- **Intrinsic Remodeling of the Fovea in Parkinson's Disease** (Markopoulou)

  - NorthShore Neurological Institute, SUNY/Michael J. Fox Foundation funds

- **Quantitative Electroencephalography as a Biomarker in Parkinson's Disease** (Narayanan)

  - NorthShore Neurological Institute/NorthShore funds

Center for Brain Health

❖ Mission: to preserve and improve brain health by preventing neurodegenerative diseases

❖ Focus on brain fitness and primary prevention

   ❖ Risk assessments (clinical, genetics, laboratory, imaging)

   ❖ Interventions (multimodal, multidisciplinary team approach)

   ❖ Surveillance (annual follow up, advanced EMR and digital health tools)

❖ Rapid translation of scientific observations and clinical trials evidence into clinical practice

❖ Visit our website: http://www.northshore.org/brainhealth

❖ Make an appointment: 1-847-503-4CBH (4224)

Neurodegenerative Disorders Program, NorthShore Neurological Institute

Thank you!

Multidisciplinary team of experts dedicated to patient centered care and the best quality and outcomes

1-847-570-7020

http://www.northshore.org/neurological-institute/